Genetically Engineered Mesenchymal Stem Cells for the Treatment of Vertebral Compression Fractures.

Grant Award Details

Genetically Engineered Mesenchymal Stem Cells for the Treatment of Vertebral Compression Fractures.

Grant Type: Disease Team Therapy Planning I

Grant Number: DR2-05288

Investigator:

Name:	Dan Gazit
Institution:	Cedars-Sinai Medical Center
Type:	PI

Disease Focus: Bone or Cartilage Disease

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Progress Reports

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Grant Application Details

Application Title: Genetically Engineered Mesenchymal Stem Cells for the Treatment of Vertebral Compression Fractures.

Public Abstract: Osteoporosis is an unsolved and highly prevalent health care problem: 10 million Americans suffer from the disease, and an additional 34 million have low bone mass. Roughly half of all women and a fourth of all men older than 50 years will sustain an osteoporosis-related fracture at some time in their lives, and when such a fracture occurs, the chances of death within 12 months are about 1 in 5. Osteoporotic fractures can take several forms, but VCFs (vertebral compression fractures) occur at a rate of 700,000 per year—twice the rate of hip fractures. The economic burden of osteoporotic fractures is tremendous. In 2001, there were approximately 1.5 million osteoporosis-related fractures in the US at a cost of $17 billion, or approximately $47 million per day. Currently, treatment is focused primarily on prevention. When fractures occur in patients with osteoporosis, treatment options are limited because open surgery with implants often fails. Recently, new therapies involving injection of cement into the vertebral body were developed. Unfortunately, these procedures do not regenerate bone tissue, but do incur risks of leakage and emboli. Moreover,recent publications in leading scientific journal question the effectiveness of those procedures. Hence, we need new biological treatment that will promote repair of such fractures in a safe and efficient manner. We propose to develop a therapy that exploits MSCs (mesenchymal stem cells) that are genetically engineered to express a bone-inducing gene, bone morphogenetic protein-2 (BMP-2). Those cells have been shown to induce bone formation and fracture repair in numerous studies in animal models. Specifically, we intend to use allogeneic ("off the shelf") human MSCs. These cells will be genetically engineered with a BMP-2 gene using a technology based on short electric pulses. BMP-2 engineered MSCs have an advantage in bone repair since they become bone cells by themselves and recruit additional cells from the environment. This synergistic effect leads to accelerated and robust bone formation, which could be an attractive therapy for a variety of clinical conditions involving bone lose. An image-guided injection of BMP-2 engineered MSCs to a fractured vertebra could be an attractive treatment that would lead to rapid fracture repair and shortening of hospitalization time. We propose to use off-the-shelf MSCs that do not require the patient to undergo additional medical procedure such as bone marrow aspiration. In addition, the use of allogeneic cells is not limited by cell number, as could be the case for autologous cells, that are taken from the patient. If successful, this therapeutic strategy could revolutionize the treatment in osteoporsis patients, offering a minimal-invasive, biological solution. We plan to analyze aspects of efficiency and safety of the proposed therapy in a pre-clinical model, that will enable us to submit an approvable IND to the FDA by the end of the 4-year project.

Statement of Benefit to California:	Approximately 10 million people in the United States are diagnosed as osteoporotic, while an additional 34 million are classified as having low bone mass. The lifetime incidence of fragility fractures secondary to osteoporosis in females over fifty years of age is approximately 1 in 2, and in males over the age of fifty, is 1 in 4. Vertebral compression fractures (VCFs) are the most common fragility fractures in the United States, accounting for approximately 700,000 injuries per year, twice the rate of hip fractures. Approximately 70,000 VCFs result in hospitalization each year with an average hospital stay per patient of 8 days. Fragility fractures due to osteoporosis also place a severe financial strain upon the health care industry. Estimates show there were approximately 1.5 million osteoporosis-related fractures in the United States in 2001, the care of which cost about $17 billion. Moreover, as the number of individuals over the age of fifty continues to increase, costs are predicted to rise to an estimated $60 billion a year by the year 2030. VCFs have previously received limited attention from the spine care community. This oversight may be a result of the perception that VCFs are benign, self-limited problems or that treatment options are limited. However, it has become clear that VCFs are associated with significant physiologic and functional impairment, even in patients not presenting for medical evaluation at the time of fracture. Current treatment of osteoporotic patients is mostly focused on prevention of VCFs. There are a few options of treatment when VCFs actually occur. Since open surgery involves morbidity and implant failure in the osteoporotic patient population, nonoperative management, including medications and bracing, is usually recommended for the vast majority of patients. Unfortunately, large numbers of patients report intractable pain and inability to return to activities. Currently there is no efficient biological solution for the treatment of VCFs. The proposed study will further develop a biological therapeutic solution that will accelerate repair of VCFs. The treatment will rely upon adult stem cell that are genetically engineered to overexpress an osteogenic gene, BMP-2, using a non-viral technique that is currently in clinical trials. It will also involve an injection of the cells into the fracture site, instead of a percutaneous injection of a polymer, which does not restore lost bone tissue. Data generated form this study could potentially revolutionize the treatment of vertebral fractures and other complex fractures in patients suffering from osteoporosis, and so benefit the citizens of California by reducing hospitalization periods, operative costs and loss of workdays, and by improving quality of life for Californians with osteoporosis that are at risk for VCFs.
